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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/821,255	03/29/2001	Michael S. C. Fung	TNX 98-2-01	7231

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TANOX, INC.
10301 STELLA LINK
HOUSTON, TX 77025

EXAMINER
DECLOUX, AMY M

ART UNIT	PAPER NUMBER
1644	14

DATE MAILED: 11/18/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/821,255	Applicant(s) FUNG ET AL.	
	Examiner Amy M. DeCloux	Art Unit 1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 August 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-21* is/are pending in the application.

4a) Of the above claim(s) *20 and 21* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *27 July 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *11* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

1. Applicant's election of Group I, claims 1-19 in Paper No. 13, filed 8-26-02, is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

2. Claims 20-21 have been withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim.

3. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Specification

4. The right inch or so of text of each of the lines of page 24 of the specification is missing, such as to make reading and examining said page difficult. A new page with the complete text is required.

Claim Rejections - 35 USC § 112

5. Claims 1-9 and 12 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

6. The instant claims are drawn to an inhibitor of complement activation which binds factor D, and encompasses an inhibitor which is a peptide, oligonucleotide, peptidomimetic, organic compound or antibody, homolog, analog or fragment thereof and cell lines producing said fragments or antibodies. However, since the Applicants have not disclosed any inhibitor or cell lines as recited in the instant claims, with the exception of the monoclonal antibody 166-32 and derivatives thereof and cell lines producing said monoclonal antibody 166-32 or fragments thereof, (see for example, page 30 of the instant specification), the invention encompassing all inhibitors and all cell lines expressing all said antibodies and derivatives thereof, is not adequately described. *see University of California v. Eli Lilly and Co. 43 USPQ2d 1398.*

7. Claims 10-19 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the

art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

8. It is apparent that monoclonal antibody 166-32 (ATCC Accession Number 12476) is required to practice the claimed invention. As a required element, it must be known and readily available to the public or obtainable by a repeatable method set forth in the specification. If it is not so obtainable or available, the enablement requirements of *35 U.S.C. 112*, first paragraph, may be satisfied by a deposit of said plasmid. *See 37 C.F.R. 1.802.* It is noted that the Applicants have disclosed on page 3-4 of the instant specification that the hybridoma producing this antibody was deposited with ATCC.

If a deposit is made under the terms of the Budapest Treaty, then an affidavit or declaration by Applicants or someone associated with the patent owner who is in a position to make such assurances, or a statement by an attorney of record over his or her signature, stating that the deposit has been made under the terms of the Budapest Treaty and that **all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent**, would satisfy the deposit requirements. *See 37 C.F.R. 1.808.*

In addition, the identifying information set forth in *37 C.F.R. 1.809 (d)* should be added to the specification. *See 37 C.F.R. 1.803-1.809* for additional explanation of these requirements,

9. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. Claims 13-14 and 16-17 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 13-14 and 16-17 are indefinite in the recitation of the phrase "is an are" in line 1 of claim 13 because it is not clear what said phrase means.

Claim Rejections - 35 USC § 102

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

12. Claims 1-7 and 12 are rejected under 35 U.S.C. 102(b) as being anticipated by Pascuel et al. (J. Immunol. Methods 127:263-269, 1990).

Pascuel et al teach a monoclonal antibody that binds Factor D and completely inhibits rabbit erythrocyte hemolysis by human serum as well as prevents the cleavage of C3 to C3b by cobra venom factor at a ratio of 80:1. (see entire article, especially the abstract). The claimed functional limitations would be inherent properties of the referenced antibodies, and one would expect at a ratio of less than 80:1, said monoclonal antibody would inhibit complement activation, though not completely. The claimed and referenced antibodies appear to have equivalent binding specificities. The burden is on the applicant to establish a patentable distinction between the claimed and referenced antibodies. See In re Best, 195 USPQ 430, 433 (CCPA 1977); In re Marosi, 218 USPQ 289, 292-293 (Fed. Cir. 1983); and In re Fitzgerald et al., 205 USPQ 594 (CCPA 1980). Therefore said reference anticipates the claimed invention.

12. Claims 1-4, and 7 are rejected under 35 U.S.C. 102(b) as being anticipated by Sahu et al (1993) (Mol. Immmunol. 30(7):679-84).

Sahu et al teach that heparin inhibits alternate pathway of complement activation in vitro (see entire article especially page 682, column 2, lines 1-8) and that factor D bound to heparin (see entire article especially page 682, column 1, last paragraph) at the concentrations recited in the instant claims since the binding occurs over 4 orders of magnitude (see entire article, especially Figure 3). Therefore said reference anticipates the claimed invention.

13. Claims 2-5 and 8-9 are rejected under 35 U.S.C. 102(b) as being anticipated by Pascuel et al (Eur. J. of Immunol. (1993) 23:1389-1392).

Pascuel et al teach a monoclonal antibody and its Fab to adipsin/factorD that binds mouse factor D which is adipsin and inhibits the alternate pathway of complement at a ratio of 42:1 (see entire article especially page 1390, column 2, paragraph 2) in vitro and in vivo as shown by an in vitro an extracorporeal assay (see entire article, especially figure 3, page 1391, column 2 paragraphs 2 and 3, and the abstract). The claimed functional limitations would be inherent properties of the referenced antibodies, absent evidence to the contrary. The claimed and referenced antibodies appear to have equivalent binding specificities. The burden is on the applicant to establish a patentable distinction between the claimed and referenced antibodies. See In re Best, 195 USPQ 430, 433 (CCPA 1977); In re Marosi, 218 USPQ 289, 292-293 (Fed. Cir. 1983); and In re Fitzgerald et al., 205 USPQ 594 (CCPA 1980). Therefore said reference anticipates the claimed invention.

Claim Rejections - 35 USC § 103

13. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

14. Claims 9, 14 and 17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pascuel et al (Eur. J. Of Immunol. (1993) 23:1389-1392 or J. Immunol. Methods 127:263-269, 1990) in view of standard techniques in the art at the time the invention was made as evidenced by Janeway et al. Immunolobiology, 3rd edition, Current Biology Ltd, London, England 1997 page 13:7-8).

Pascuel et al teach as above.

Pascuel et al do not teach a chimeric, humanized, deimmunized or human form of the antibody or cell line producing said antibody.

Janeway et al teaches standard techniques in the art at the time the invention was made including that humanized antibodies comprise the CDRs of a mouse monoclonal antibody onto the human framework of a human immunoglobulin, and that said chimeric antibodies are far less immunogenic in humans than the parent mouse monoclonal antibodies, and thus they can be used for treatment of humans with far less risk of anaphylaxis than the parent non-human monoclonal antibodies. For similar purposes, monoclonal antibodies that are entirely human in origin can be made in mice lacking endogenous immunoglobulin genes.

Therefore, one of ordinary skill in the art at the time the invention was made, who wanted to decrease the negative effects of complement in patients with pathological inflammation and autoimmune disease, would have been motivated to make and use the chimeric and/or human form and recombinant cell lines thereof, taught by Janeway et al. of the monoclonal antibodies taught by Pascuel et al. as an inhibitor of complement activation because Janeway et al teaches that humanized antibodies are far less immunogenic in humans and have far less risk of anaphylaxis and because Pascuel teaches a monoclonal antibody that binds Factor D and inhibits complement activation.

From the teachings of the references, it was apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

One of ordinary skill in the art at the time the invention was made would have been motivated to use the chimeric form of the monoclonal antibodies taught by Pascuel et al as an inhibitor of the alternate pathway of complement activation because Janeway et al teaches that humanized antibodies are far less immunogenic in humans and have far less risk of anaphylaxis.

15. Claims 8, 13, 15 and 16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pascuel et al (Eur. J. Of Immunol. (1993) 23:1389-1392 or J. Immunol. Methods 127:263-269, 1990) in view of U.S. Patent No. 5,861,156.

Pascuel et al teach as above.

Pascuel et al do not teach the recited antibody fragments nor a cell line that produces daid fragments.

'156 teaches in Column 10, lines 42-62, that the complete antigen binding site of an antibody may be obtained by recombinant methods from monoclonal antibodies or combinatorial libraries, and may correspond to the two-chain 50 kD Fab or related Fab' fragments, the two-chain 25 kD Fv fragment, or the 26-27 kD single-chain Fv. '156 teaches that all of these species are smaller and far more rapid in biodistribution than IgG monomers or dimmers and that their reduced size is advantageous for primary targeting.

Therefore, one of ordinary skill in the art at the time the invention was made, who wanted to decrease the negative effects of complement in patients with pathological inflammation and autoimmune disease, would have been motivated to make and use the Fab, $F(ab)_2$, Fv or ScFv forms and recombinant cell lines thereof, taught by '156 of the monoclonal antibodies taught by Pascuel et al. as an inhibitor of complement activation because '156 et al teaches that antibody are smaller and far more rapid in biodistribution than IgG monomers or dimmers and that their reduced is advantageous for primary targeting, and because Pascuel teaches a monoclonal antibody that binds Factor D and inhibits complement activation.

From the teachings of the references, it was apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Conclusion

No Claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amy M. DeCloux whose telephone number is 703 306-5821. The examiner can normally be reached on M-F 8:00-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 703 308-3973. The fax phone numbers for the organization where this application or proceeding is assigned are 703 305-3014 for regular communications and 703 872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703 308-0196.

Amy DeCloux, Ph.D.
Patent Examiner
November 13, 2002

Patrick J. Nolan, Ph.D.
Primary Patent Examiner
Group 1640